

TRANSLATION**PATENT COOPERATION TREATY****PCT****INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY**

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference H 8017/zi	FOR FURTHER ACTION	See Form PCT/IPEA/416
International application No. PCT/AT2005/000107	International filing date (day/month/year) 24.03.2005	Priority date (day/month/year) 29.03.2004
International Patent Classification (IPC) or national classification and IPC A61K38/00		
Applicant HALLSTRÖM, Seth		

<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of _____ sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input checked="" type="checkbox"/> (sent to the applicant and to the International Bureau) a total of <u>2</u> sheets, as follows:</p> <p><input checked="" type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>																									
<p>4. This report contains indications relating to the following items:</p> <table><tr><td><input checked="" type="checkbox"/></td><td>Box No. I</td><td>Basis of the report</td></tr><tr><td><input type="checkbox"/></td><td>Box No. II</td><td>Priority</td></tr><tr><td><input checked="" type="checkbox"/></td><td>Box No. III</td><td>Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td></tr><tr><td><input checked="" type="checkbox"/></td><td>Box No. IV</td><td>Lack of unity of invention</td></tr><tr><td><input checked="" type="checkbox"/></td><td>Box No. V</td><td>Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</td></tr><tr><td><input type="checkbox"/></td><td>Box No. VI</td><td>Certain documents cited</td></tr><tr><td><input type="checkbox"/></td><td>Box No. VII</td><td>Certain defects in the international application</td></tr><tr><td><input type="checkbox"/></td><td>Box No. VIII</td><td>Certain observations on the international application</td></tr></table>		<input checked="" type="checkbox"/>	Box No. I	Basis of the report	<input type="checkbox"/>	Box No. II	Priority	<input checked="" type="checkbox"/>	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability	<input checked="" type="checkbox"/>	Box No. IV	Lack of unity of invention	<input checked="" type="checkbox"/>	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement	<input type="checkbox"/>	Box No. VI	Certain documents cited	<input type="checkbox"/>	Box No. VII	Certain defects in the international application	<input type="checkbox"/>	Box No. VIII	Certain observations on the international application
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Date of submission of the demand	Date of completion of this report																								
Name and mailing address of the IPEA/EP	Authorized officer																								
Facsimile No.	Telephone No.																								

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/AT2005/000107

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language _____ which is the language of a translation furnished for the purposes of:
- ☐ international search (Rule 12.3 and 23.1(b))
- ☐ publication of the international application (Rule 12.4)
- ☐ international preliminary examination (Rule 55.2 and/or 55.3)
2. With regard to the **elements** of the international application, this report is based on (*replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report*):
- ☐ the international application as originally filed/furnished
- ☒ the description:
- pages 1-16 _____ as originally filed/furnished
- pages* _____ received by this Authority on _____
- pages* _____ received by this Authority on _____
- ☒ the claims:
- nos. _____ as originally filed/furnished
- nos.* _____ as amended (together with any statement) under Article 19
- nos.* 1-7 _____ received by this Authority on 30.01.2006 with letter
- nos.* _____ received by this Authority on of 29.01.2006
- ☒ the drawings:
- sheets 1/8-8/8 _____ as originally filed/furnished
- sheets* _____ received by this Authority on _____
- sheets* _____ received by this Authority on _____
- ☐ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.
3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages _____
- ☐ the claims, nos. _____
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing (*specify*): _____
- ☐ any table(s) related to sequence listing (*specify*): _____
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages _____
- ☐ the claims, nos. _____
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing (*specify*): _____
- ☐ any table(s) related to sequence listing (*specify*): _____

* If item 4 applies, some or all of those sheets may be marked "superseded."

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/AT2005/000107

Box No. III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application
- ☒ claims Nos. 1-4, 6, 7 (in part)

because:

- ☐ the said international application, or the said claims Nos. _____
relate to the following subject matter which does not require an international preliminary examination (*specify*):

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. _____
are so unclear that no meaningful opinion could be formed (*specify*):

- ☐ the claims, or said claims Nos. _____ are so inadequately supported
by the description that no meaningful opinion could be formed.

- ☒ no international search report has been established for said claims Nos. 1-4, 6, 7 (in part)

- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

- ☐ has not been furnished
- ☐ does not comply with the standard

the computer readable form

- ☐ has not been furnished
- ☐ does not comply with the standard

- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

- ☒ See Supplemental Box for further details.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/AT2005/000107

Box No. IV

Lack of unity of invention

1. ☒ In response to the invitation to restrict or pay additional fees the applicant has:
- ☐ restricted the claims.
 - ☐ paid additional fees.
 - ☐ paid additional fees under protest.
 - ☒ neither restricted the claims nor paid additional fees.
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is:
- ☐ complied with.
 - ☒ not complied with for the following reasons:

See supplemental sheet

4. Consequently, this report has been established in respect of the following parts of the international application:
- ☐ all parts.
 - ☒ the parts relating to claims Nos. 1-4, 6, 7 (in part), 5 (in full) (of the first invention mentioned in the claims).

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/AT2005/000107

Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement		
1. Statement			
Novelty (N)	Claims	<u>1-7</u>	YES
	Claims	<u>-</u>	NO
Inventive step (IS)	Claims	<u>1-7</u>	YES
	Claims	<u>-</u>	NO
Industrial applicability (IA)	Claims	<u>1-7</u>	YES
	Claims	<u>-</u>	NO
2. Citations and explanations (Rule 70.7)			
<p>The opinion established with regard to novelty, inventive step and industrial applicability only relates to those parts of the application for which an international search report has been established (see Boxes III, IV).</p> <p>Reference is made to the following document:</p> <p>D1: WO 01/65935 A (VODOVOTZ YORAM; GAGE FREDERICK A) 13 September 2001</p> <p><u>1. Amendments (PCT Article 34(2)(b))</u></p> <p>The novel set of patent claims filed with the communication of 29.01.2006 is admissible because it contains no substantive matter that goes beyond the disclosure content of the international application at the time of filing.</p> <p><u>2. Novelty and inventive step (PCT Article 33(2), 33(3))</u></p> <p>Invention 1 of the present application relates to the use of the therapeutic protein S-nitroso-albumin and of the compound glutathione, which comprises thiol groups, for</p>			

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/AT2005/000107

Box No. V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;
citations and explanations supporting such statement

the preparation of a pharmaceutical combined preparation for the **treatment** of damage caused by ischaemia and reperfusion, of shock, thrombotic states, diseases of the respiratory system, erectile dysfunctions and hypertension.

While **D1** discloses such a pharmaceutical combined preparation, it is used for the **prevention** of the damage, caused by ischaemia and reperfusion, of a kidney to be transplanted, which is done by perfusing the kidney prior to the transplantation.

However, a therapeutical application for damage caused by ischaemia and reperfusion is neither disclosed nor suggested in D1.

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of:

Box III

1. The extent of the international search has been restricted as follows:

The original **patent claims 1, 2, 7** relate to an inordinately large number of possible combined preparations. In fact they encompass so many alternatives (several million different combinations) that they appear unclear and too broadly worded (PCT Article 6) to the extent that it was impossible to conduct a meaningful search. Moreover, the patent claims encompass a very large number of different combined preparations, whereas the patent application, with the description, only supports a very limited number of such preparations (PCT Article 5). In the present case the claims lack the proper support and the application lacks the requisite disclosure to such an extent that it does not appear possible to carry out a meaningful search covering the entire range of protection sought. The search was therefore directed to the parts of the claims that appear to be clear, namely combined preparations which contain a combination of the proteins and compounds mentioned in claims 3 and 4.

The International Preliminary Examining Authority agrees with this restriction put in place by the International Searching Authority.

2. Moreover, the present international application does

Supplemental Box

not meet the criteria for unity of invention which are specified in PCT Rule 13.1 and 13.2.

Pursuant to PCT Article 17(3)(a), the international search report was established for those parts of the application which relate to the first invention mentioned in the patent claims, namely the subject matter of **claims 1-4, 6, 7 (in part) and 5 (in full)**, which is a combined preparation comprising S-nitroso-albumin as the therapeutic protein and glutathione as the compound comprising thiol groups. No international search report has been established for the inventions 2-36 (**claims 1-4, 6, 7 (in part)**) (see PCT/ISA/form 206).

Again, the International Preliminary Examining Authority agrees with this restriction put in place by the International Searching Authority (see Box IV).

3. The applicant is advised that claims relating to inventions in respect of which no international search report has been established cannot normally be the subject of an international preliminary examination (PCT Rule 66.1(e)). In its capacity as International Preliminary Examining Authority the EPO generally will not carry out a preliminary examination for subjects that have not been searched. This also applies to cases where the claims were amended after receipt of the international search report (PCT Article 19) or where the applicant submits new claims in the course of the procedure under PCT Chapter II.

Supplemental Box

Consequently, the searched subject matter of the first invention, namely a combined preparation comprising S-nitroso-albumin as the therapeutic protein and glutathione as the compound comprising thiol groups **(claims 1-4, 6, 7 (in part) and 5 (in full))** forms the basis for the reasoned statement with regard to novelty, inventive step and industrial applicability (see Box V).

Box IV

The International Searching Authority has found that the present international application contains several inventions, or groups of inventions, which are not linked by a special technical feature (PCT Rule 13.2) or by a single general inventive concept (PCT Rule 13.1) (see form PCT/ISA/210).

The objection on the grounds of lack of unity of invention is sustained by the International Preliminary Examining Authority, for the following reasons:

The inventions relate to combined preparations which contain a therapeutic protein with SH groups that are nitrosated and a compound comprising thiol groups and having an average molecular weight of no greater than 10 000.

The single concept which links the inventions is that combined preparations with the above-described chemical character can be employed for improving perfusion or microcirculation, for example in the case of ischaemia, reperfusion damage, transplants and surgical intervention

Supplemental Box

with subsequent reperfusion.

Combined preparations with the above-described chemical character for improving perfusion or microcirculation, specifically for the purposes of transplant surgery, have already been described in the prior art. WO0165935 describes a combined preparation which contains, *inter alia*, S-nitroso-albumin as the therapeutical protein and glutathione as the thiol-containing compound (see claims 1-3).

In the light of this prior art, the problem to be addressed by the present application can thus be considered that of providing additional combined preparations with the above-described chemical character for improving perfusion or microcirculation.

The combined preparations which are mentioned in inventions 1-36 (see PCT/ISA/form 206) constitute different solutions of the abovementioned problem.

Taking into consideration that combined preparations with the above-described chemical character for improving perfusion or microcirculation have already been described in the prior art, and taking into consideration the lack of other technical features which might be considered as special technical features, it has been found that the 36 claimed inventions of the present application are not based on a single general inventive concept within the meaning of PCT Rule 13.1. Consequently, lack of unity of invention exists.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/AT2005/000107

Supplemental Box

The International Preliminary Examining Authority retains the grouping of inventions as carried out by the International Searching Authority (see PCT/ISA/form 206).

Pursuant to PCT Article 17(3)(a), the international search report was prepared for those parts of the application which relate to the first invention mentioned in the claims, namely the subject matter of **claims 1-4, 6, 7 (in part), 5 (in full)**. Consequently, the searched subject matter of the first invention, namely a combined preparation containing S-nitroso-albumin as the therapeutic protein and glutathione as the compound comprising thiol groups forms the basis for the reasoned statement with regard to novelty, inventive step and industrial applicability (see Box V).